III. Remarks

Claims 5-9, 14, 16-17, and 23-25 are presently pending. Claims 18-22 were cancelled without prejudice or disclaimer in response to the Final Rejection of November 17, 2004. Claims 1-4, 10-13 and 15 are withdrawn from consideration as directed towards the non-elected invention. Claim 5 has been amended.

Applicant extends its thanks to Examiner Parkin for the interview of January 27, 2005. Agreement was reached and this response embodies that agreement.

Only one rejection remains in this case, the 35 USC §112, first paragraph rejection, i.e., the "written description" rejection. Applicants respectfully request reconsideration of the rejection based upon the claim amendment and the following argument. The response will concentrate on four main topics:

1) To begin, a summary of the rejections made by the Examiner are useful.

2) Then, an analysis of the case law about the written description requirements it applies to:

   a. the guidelines issued by the USPTO itself on the interpretation of the written description requirements;

   b. the CAFC decision ***Enzo v. Gen-Probe***; and,

   c. the MPEP, as to the "description" of a micro-organism in a patent application (extracted from the ***Enzo v. Gen-Probe*** decision).

3) Third, in addition to the technical documents already on file, documents are herein provided that further demonstrate the techniques used in the present invention are

art-recognized techniques for characterization of micro-organisms, in particular of viruses, and, thus, that these techniques unambiguously prove the "possession" of the invention when the application was filed.

4) Fourth, and finally, the specification both from a quantitative- and qualitative point-of-view provides technical information and guidance that (is more than sufficient to) demonstrate "possession" of a genus of ERS strains/isolates.

The Examiner's Rejections:

The Examiner questions whether the application provides adequate support for the broadly claimed genus of avian reoviruses. The Examiner's primary contention is that the invention may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no art-recognized correlation or relationship between the structure of the invention and its function.

Case Law Analysis:

a. The USPTO written description guidelines

Example 9 of the MPEP (Hybridization)

In this example, a single cDNA sequence (SEQ NO: 1) is disclosed that is said to hybridize to other nucleic acids under stringent conditions and these nucleic acids also encode a protein that binds with a certain receptor.

The claim is directed to a genus of nucleic acids all of which must hybridize with SEQ NO: 1 under highly stringent conditions.

The guidelines reason such complies with the written description requirement using the following reasoning:

- Hybridization techniques using DNA as a probe were conventional in the art.
- A single species is disclosed that is actual reduced to practice.
- The skilled person would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent conditions mentioned in the claim yield structural similar DNAs.

Thus, in conclusion, a representative number of species is disclosed, as the hybridization conditions in combination with the coding function and the level of skill and knowledge in the art adequately determine possession. Much the same as the present case.

Example 14 of the MPEP (Product by function)

A protein having an amino acid sequence as in SEQ NO: 3 is disclosed that in addition has the property to catalyze a certain reaction. Variants (at least 95% identical) of the protein are contemplated but not exemplified. Procedures for making such variants are conventional and an assay to determine the catalytic activity is described. The claim is directed to SEQ NO: 3 and its variants (at least 95% identical and having the catalytic activity).

The guidelines reason such complies with the written description requirement using the following reasoning:

- There is actual reduction to practice of the single species.

- The genus of variants do not have substantial variation as the amino acid sequence of variants is at least 95% identical and have the specified catalytic activity.

Thus, in conclusion, the single species is representative of the genus because of these limitations and of the presence of the assay.

Example 16 Antibodies

An antigen X has been isolated and characterized. The specification contemplates but does not teach in an example any antibody which specifically binds to the antigen. The general knowledge in the art is such that antibodies are structurally well characterized, e.g. antibodies contain antigen binding sites in the form of complementary (to the antigen) determining regions. The claim is directed to antibodies that are capable of binding to antigen X.

The guidelines reason such complies with the written description requirement using the following reasoning:

- Again, the level of skill and knowledge in the art (of antibodies) is deemed important, leading to the conclusion that this level was such that the production of antibodies against a well characterized antigen was conventional.
- Considering the routine methods of making antibodies, the well defined structural characteristics of antibodies, including the functional characteristics of antibody binding requirements, the skilled person would recognize that the spectrum of antibodies that bind to antigen X are disclosed as a result of the isolation of antigen X.

Thus, in conclusion, the MPEP provides guidance that once a specie is disclosed also variants of such a specie that do not substantial differ structurally from that specie are described.

b. The CAFC decision ***Enzo v. Gen-Probe***

The present case, as well as the ***Enzo v. Gen-Probe*** case, is distinguished from the Eli Lilly case (heavily relied on by the Examiner in examination of Applicants' claims). In ***Eli Lilly***, it was held that in case (a gene) material has been defined only by a statement of function or result, such statements alone did not adequately describe that material.

In contrast, Applicants invention is a claim of:

(i) the "avian reovirus" , in combination with

(ii) the immunogenic properties as defined in the claims.

Applicants contend such represents a precise definition of the claimed subject-matter as to its structural- and physical characteristics, and that this case for exactly this reason, is distinguished from the ***Eli Lilly*** case.

The ***Enzo*** Court held that:

"*It is not correct, however, that all functional descriptions of genetic material fail to meet the written description requirement*", and referring to the MPEP that the written description requirement can be met by "*showing....sufficiently detailed, relevant identifying characteristics, e.g. functional characteristics when coupled with a known or disclosed correlation between function and structure..*" (page 5, 1st full paragraph).

The ***Enzo***-court also referred to Example16 of the USPTO written description guidelines: antibodies are adequately described by means of their binding property with a certain antigen, because this binding property implies well defined structural characteristics of such antibodies. ***See Enzo Biochem Inc. v. Gen-Probe Inc.***, 63 USPQ2d 1609, 1613 (CA FC 2002).

Although the Court did not decide on the fulfillment of the written description requirement for those claims that cover a genus of nucleotide sequences, because this is a matter of fact specific to the case, it nevertheless provided guidance how (for the District Court) to assess such a question, an such guidance applies to the USPTO:

In ***Ely Lilly*** the specification "*did not set forth any common feature possessed by members of the genus that distinguished them from other*".

Notably, the ***Enzo***-court specifically refers to Example 9 of the written description guidelines that mirrors the ***Enzo***-case in that the Example 9 also concerns a genus claim to nucleic acids based on their hybridizing properties. As already outlined above, the USPTO guidelines determined that such a genus claim fulfilled the written description guidelines, because all species within the genus will be structurally similar.

In other words, the Enzo-court approaches the same question from another side: nucleotide sequences that preferentially bind to the described genomic DNA of certain deposited bacteria may also be adequately described because such sequences have a (complementary) structural relationship with the genomic DNA. ***See Id.*** at 1693-4. This reasoning is very similar to the Antibody-Antigen Example 16 in the written description guidelines.

c. The MPEP, as to how to describe a micro-organism in a patent application (interpreted in the ***Enzo v. Gen-Probe*** decision)

The ***Enzo***-court makes perfectly clear that practical difficulties are associated with describing unique biological materials in a written description and stresses both the importance and well accepted practice before the USPTO of depositing a sample of the micro-organism to satisfy the §112, 1st paragraph requirements, including the written description requirement:

"..we hold that reference in the specification to a deposit in a public depository, which makes its contents accessible to the public when it is not otherwise available in written form, constitutes an adequate description of the deposited material sufficient to comply with the written description requirement of §112, 1". **See Id.** at 1613. The Enzo-court held that micro-organisms "are adequately described in the specification by their accession numbers" and that a description of a micro-organism by virtue of its genomic sequence (which would be unduly burdensome, because it would take 3000 scientists one month to sequence the genome of one micro-organism) is by no means a prerequisite for satisfying the written description requirement. ***See Id.*** Clearly, the ***Enzo***-court is of the opinion that the description of a biomolecule is something different than the description of a complex biological material, such as a micro-organism, and that the deposit of biological material is a well established manner to describe such material.

The Techniques Used by Applicants are art accepted:

The documents previously submitted and the following documents unambiguously demonstrate that a plaque reduction assay (based on virus neutralization

by antiserum) is a conventional test that demonstrates antigenic similarity between related viruses in a very specific and selective manner (see the various previous citations in the responses). Further, when compiled with a monoclonal binding panel pattern, complete disclosure is made and one of ordinary skill in the art has the invention.

The tests provide functional characteristics, i.e. (i) the neutralization of a virus by antiserum or (ii) the binding of a monoclonal antibody to the virus and, importantly, the tests correlate directly with the structure of the viruses, i.e. the presence or absence of certain antigenic determinants or epitopes on the surface of the virus. In other words, the tests provide an art-recognized correlation or relationship between the function and structure. The tests provide information on the phenotypical properties of the virus (presence/absence of certain antigenic determinants) and, hence, on the genotypical properties of the virus, i.e. the presence /absence of the corresponding coding sequences for these antigenic determinants.

Serological tests based on virus neutralization or binding with monoclonal antibodies are not just random tests, but are the tests utilized in this artfield to demonstrate (structural) similarity between species within a genus and to distinguish these species from structurally unrelated antigens/species.

The neutralization of a virus by a certain antiserum or the binding pattern of a panel of monoclonal antibodies provide an "antigenic fingerprint" of the virus, and as such structurally characterizes the species within a genus of genotypically/phenotypically homogeneous virus isolates.

Importantly, it is noted that also the term "avian reovirus" used in the claims, inherently, defines the claimed subject-matter in a structural manner, as the claimed virus comprises the known structural properties of an avian reovirus. For example, virion properties of reoviruses, and avian reoviruses in particular, are disclosed in the following textbook:

Virus Infections Of Birds, eds.: Mc Ferran and McNulty, Elsevier Science Publishers B.V., 1993, pages 177 and 181. (previously submitted to the Examiner).

Applicants have Possession of the Claimed Invention:

Applicants have amended Claim 5 to incorporate the limitations of the monoclonal binding pattern and the plaque reduction assay. Claim 5 now reads "[a] vaccine comprising an isolated avian reovirus belonging to an antigenic class of avian ERS reoviruses wherein the avian reovirus is able to induce antiserum in an animal, which antiserum causes a reduction of the plaques formed by avian reovirus ERS(isolate 1), deposited at the ECACC under accession no. 99011475, of at least 75% in a plaque reduction assay and wherein the avian reovirus positively reacts with polyclonal avian reovirus antiserum raised against strain 1133, but not with monoclonal antibodies identified by accessions nos. 99011472, 99011473 and 99011474, samples of which are deposited at the ECAC, and a pharmaceutical acceptable carrier or diluent." Accordingly, Applicants have further defined their invention. However, the amendment does not limit the scope of the claim and will not effect the application of the doctrine of equivalents because such amendment was inherent in the disclosure. The ERS type isolate of an avian reovirus is identified by both the monoclonal binding pattern and the

plaque reduction assay of the present invention. Accordingly, Applicants respectfully request reconsideration.

Moreover, the specification on page 6 of the present invention and Example 1A provide the method and the tools to the skilled person to isolate and identify the new ERS isolates. Further, Examples 1B-C disclose 13 identified representatives. As well, Tables 2A and B indeed prove (as outlined above) that the antiserum raised against prior art, non-ERS isolates is not able to cause plaque reduction of ERS isolates, whereas antiserum raised against an ERS isolate is able to reduce the plaques of the specifically deposited ERS isolate (ERS-1, see also page 7, last paragraph).

In addition, the (Moab) binding pattern as specified in the Claims further defines the antigenic/structural properties of the claimed ERS isolates. The Moab reaction pattern makes clear that the claimed ERS isolates:

(i) bind with polyclonal anti-avian reovirus antiserum (and with certain Moabs that apparently bind with antigenic determinants that are conserved in all avian reoviruses), but

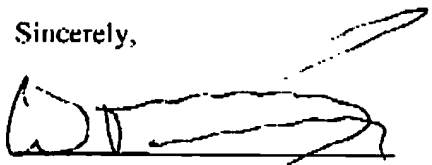
(ii) do not bind with the three specified Moabs INT-14-11, INT-13-06 and 15-01 INT. This functional property of the claimed ERS isolates implies that ERS isolates do not have these antigenic determinants that are present on known avian reoviruses.

In conclusion, the Claims are in compliance with the USPTO's written description guidelines and the guidance provided by the ***Enzo***-Court, the skilled person would directly recognize the spectrum of claimed ERS isolates and that the inventors were in the possession of a genus of ERS isolates that do not substantially differ structurally.

IV. CONCLUSION

In light of the argument above, Applicants respectfully request reconsideration of the rejection and allowance of the case. Applicants further respectfully request that a personal interview be granted between Applicants' attorney and the Examiner. Please charge any required fees to deposit account 02-2334 and credit any credits.

Sincerely,



William P. Ramey, III
Reg. No. 44,295

Akzo Nobel Pharma Patent Department
29160 Intervet Lane
P.O. Box 318
Millsboro, DE 19966
Tel: (302) 933-4034
Fax: (302) 934-4305